Office Action Summary	Application No.	Applicant(s)	
	10/524,520	LOIBNER ET AL.	
	Examiner	Art Unit	
	BRADLEY DUFFY	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-10,12-15,17-22,25-27,29,32,34-43 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10,12-15,17-22,25-27,29,32,34-43 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20091204* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed August 17, 2009, is acknowledged and has been entered. Claims 1, 17, 26, 29 and 48 have been amended. Claims 30-31 and 49 have been cancelled.

2. Claims 1-5, 7-10, 12-15, 17-22, 25-27, 29, 32, 34-43 and 46-48 are pending in the application and are under examination.

Grounds of Objection and Rejection Withdrawn

3. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed April 16, 2009, have been obviated or rendered moot by Applicant's amendment and/or arguments filed August 17, 2009. Notably, copending Application No. 10/558,166 is now abandoned so the previous double patenting rejection is now moot.

New Grounds of Objection

Claim Objections

4. Claim 27 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In this case, claim 26 has been amended in the response filed August 17, 2009, to recite "said antigen is Lewis Y". Accordingly, claim 27 which depends from claim 26 and which also recites "said antigen is Lewis Y" does not properly limit claim 26. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Appropriate correction is required.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 102

5 The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The rejection of claims 1-5, 7-8, 10, 12-15, 18-19, 22, 46 and 48 under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,716,595 (of record), is maintained.

At page 9 of the amendment filed August 17, 2009, Applicant has traversed this ground of rejection.

In this traversal, Applicant appears to be arguing that amending the claims to recite "functionally active antibody" renders the claims novel over the teachings of US Patent No. 5,716,595 because the "antibody modifications [of US Patent No. 5,716,595] lead to an impairment of [antibody] activity" (see third paragraph page 9). Applicant further appears to argue that the antibody conjugates of US Patent No. 5,716,595 administered during surgery would be inoperable because of this impairment of activity and because US Patent No. 5,716,595 does not demonstrate therapeutic activity of the antibodies conjugates in inhibiting tumor cell dissemination.

In response, while Applicant's argument regarding the inoperability of the prior art is acknowledged, the applicant is directed to MPEP 716.01 (C) I and II wherein it states that:

> Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results, commercial success, solution of a long-felt need, ***inoperability of the prior art***, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("It is well settled that unexpected results must. be established by factual evidence." See also In re Lindner, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972); Ex parte George, 21 USPQ2d 1058 (Bd. Pat. App. & Inter. 1991). The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results,

> commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See MPEP § 2145 generally for case law pertinent to the consideration of applicant's rebuttal arguments.[1]

Thus, as will be discussed in more detail below, Applicant's argument that the prior art is inoperable is not found persuasive.

Notably, as set forth in MPEP 2121, efficacy is not a requirement for prior art enablement. MPEP 2121, Section III states:

> A prior art reference provides an enabling disclosure and thus anticipates a claimed invention if the reference describes the claimed invention in sufficient detail to enable a person of ordinary skill in the art to carry out the claimed invention; "proof of efficacy is not required for a prior art reference to be enabling for purposes of anticipation." Impax Labs. Inc. v. Aventis Pharm . Inc., 468 F.3d 1366, 1383, 81 USPQ2d 1001, 1013 (Fed. Cir. 2006). See also MPEP § 2122.

In this case, US Patent No. 5,716,595 teaches administration of antibodies that are encompassed by the scope of the claimed "functionally active antibodies" because the antibody conjugates of US Patent No. 5,716,595 would retain at least some functional activity, i.e., ability to bind antigen and other activities, and Applicant has not submitted any evidence to reasonably establish that the antibody conjugates of US Patent No. 5,716,595 are not capable of activating antibody-dependent cellular cytotoxicity and complement dependent cytotoxicity effector functions to inhibit tumor cell dissemination. In this case, the evidence relied upon (see Antibody Labeling Overview submitted 8/17/09) does not establish that the antibody conjugates of US Patent No. 5,716,595 lose all functions, i.e., are not "functionally active antibodies" and therefore Applicant's argument is not persuasive.

Notably, the Office does not have the facilities for examining and comparing the antibody conjugates of the prior art in order to establish that the antibody conjugates of the prior art do not possess the same material, structural, and functional characteristics as Applicant's "functionally active antibodies". In the absence of evidence to the contrary, the burden is upon the applicant to prove that the antibody used in the method to which the claims are directed is different than that taught by the prior art. See *In re*

[1] Emphasis added

Best, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

For these reasons, the processes of US Patent No. 5,716,595 remain manipulatively and materially indistinguishable from the claimed processes. Thus, absent a showing of any difference, the claimed processes are still deemed to be anticipated by the prior art.

Accordingly, while Applicant's arguments have been carefully and completely considered it is for these reasons and as further explained in the previous Office actions, that the rejection of claims 1-5, 7-8, 10, 12-15, 18-19, 22, 46 and 48 under 35 U.S.C. 102(b), as being anticipated by US Patent No. 5,716,595, is maintained.

7. The rejection of claims 1-5, 7-8, 10, 12-15, 18-19 and 48 under 35 U.S.C. 102(b) as being anticipated by US Patent No. 6,107,102 (of record), is maintained.

At page 9 of the amendment filed August 17, 2009, Applicant has traversed this ground of rejection.

In this traversal, Applicant reiterates their arguments in regard to US Patent No. 5,716,595 because US Patent No. 6,107,102 also teaches administration of a conjugated antibody during surgery.

In response, these arguments are not found persuasive for the same reasons set forth in the above rejection and the Examiner herein incorporates and applies this reasoning to this rejection of the claims as being anticipated by US Patent No. 6,107,102.

Based on this reasoning, the processes of US Patent No. 6,107,102 remain manipulatively and materially indistinguishable from the claimed processes. Thus, absent a showing of any difference, the claimed processes are still deemed to be anticipated by the prior art.

Accordingly, while Applicant's arguments have been carefully and completely considered it is for these reasons and as further explained in the previous Office actions, that the rejection of claims 1-5, 7-8, 10, 12-15, 18-19 and 48 under 35 U.S.C. 102(b), as being anticipated by US Patent No. 6,107,102, is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. The rejection of claims 1, 9, 17, 20, 25-27, 29, 32, 35-40, 43 and 47 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,716,595 (Goldenberg et al, published 1998) (of record), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) (of record) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000) (of record), is

maintained.

At page 12 of the amendment filed August 17, 2009, Applicant has traversed this ground of rejection.

In this traversal, Applicant appears to be arguing that Schlimok et al and Crisan et al teach away from the claimed invention, citing *McGinley v. Franklin Sports*, Inc., 262 F.3d 1339, 1354 [60 USPQ2d 1001] (Fed, Cir. 2001) for the proposition that "[a] reference may teach away from a use when that use would render the result inoperable".

In response, *McGinley v. Franklin Sports*, Inc., 262 F.3d 1339, 1354 [60 USPQ2d 1001] (Fed, Cir. 2001) appear to be distinguished from the instant case as the Examiner could not find support for the proposition that "[a] reference may teach away from a use when that use would render the result inoperable".

In *McGinley v. Franklin Sports* the closest approximation of this proposition appears to occur when the Court sets forth:

> Perhaps McGinley's best argument to save his claims from prima facie obviousness in the light of Pratt and Morgan is his contention that those references together teach away from their combination. We have noted elsewhere, as a "useful general rule," that references that teach away cannot serve to create a prima facie case of obviousness. In re Gurley, 27 F.3d 551, 553, 31 USPQ2d 1131, 1132 (Fed. Cir. 1994). If references taken in combination would produce a "seemingly inoperative device," we have held that such references teach away from the combination and thus cannot serve as predicates for a prima facie case of obviousness. In re Sponnoble, 405 F.2d 578, 587, 160 USPQ 237, 244 (CCPA 1969) (references teach away from combination if combination produces seemingly inoperative device); see also In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984) (inoperable modification teaches away).

However, the instant case is distinguished from this reasoning as the obviousness rejection is not based on the combination of the references to produce a device that is a combination of two starting devices.

Instead, as set forth in the previous office action, the obviousness rejection is based on Schlimok et al teaching that ***disseminated*** breast epithelial tumor cells express a surface antigen designated Lewis Y by detecting immunocomplexes of Lewis Y and a Lewis Y antibody and that ***administering preparations of Lewis Y antibodies*** in buffers to breast cancer patients systemically in doses of 100 mg ***inhibits tumor cell***

dissemination in patients with large numbers of disseminated tumor cells present in their bone marrow (see entire document, e.g., abstract, page 1802, Tables 3 and 4) and Crisan et al teaching that breast tumor epithelial cells can be mobilized to disseminate from the tumor site **during** breast surgery as patients monitored for disseminated tumor cells before and after breast surgery show increased levels of circulating disseminated cells after surgery (see entire document, e.g. abstract and page 36, left column).

In this case, while Applicant appears to argue that the ***Lewis Y antibodies*** would be inoperable in the methods of Goldenberg et al, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the method of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Accordingly, because Crisan teaches that surgery ***increases*** the number of disseminated tumor cells, while Schlimok teaches Lewis Y antibodies that ***inhibit dissemination of tumor cells***, one of skill in the art would not have found it inventive to administer such antibodies ***during surgery*** to inhibit tumor cell dissemination because one of skill in the art would have immediately recognized that there was a predictable solution to solve the art known problem of surgery **increasing dissemination** of tumor cells expressing Lewis Y antigen, i.e., administering Lewis Y antibodies during surgery because such antibodies were known in the art to inhibit tumor cell dissemination in view of the prior art as a whole.

Accordingly, because the references as a whole suggest and provide motivation for one of skill in the art to administer Lewis Y antibodies during surgery to inhibit tumor cell dissemination, it is submitted that the references do not teach away from the claimed invention. Therefore, after considering the prior art as a whole, after carefully and fully considering Applicant's response and for the reasons of record set forth in the previous office action, the invention as a whole was obvious to one of ordinary skill in

the art at the time the invention was made, as evidenced by the references and this rejection is maintained.

11. The rejection of claims 21, 34, 41 and 42 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,716,595 (Goldenberg et al, published 1998) (of record), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) (of record) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000) (of record) as applied to claims 1, 9, 17, 20, 25-27, 29, 32, 35-36 and 38-40 above, and further in view of US Patent 5,792,456 (Yelton et al, published 1998) (of record), is maintained.

At page 12 of the amendment filed August 17, 2009, Applicant has traversed this ground of rejection.

In this traversal, Applicant relies on the same arguments which were not found persuasive in the above rejection under 35 U.S.C. 103(a).

As applied to this rejection these arguments also are not found persuasive for the same reasons as explained above and the Examiner herein incorporates the above reasoning into this rejection.

Accordingly, after considering the prior art as a whole, after carefully and fully considering Applicant's response and for the reasons of record set forth in the previous office action, the invention as a whole was obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and this rejection is maintained.

12. The rejection of claims 1, 9, 17, 20, 25-27, 29, 32, 35-40, 43 and 47 under 35 U.S.C. 103(a) as being unpatentable over by US Patent 6,107,102 (Ferrari et al, published 2000) (of record), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) (of record) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000) (of record), is maintained.

At page 12 of the amendment filed August 17, 2009, Applicant has traversed this ground of rejection.

In this traversal, Applicant relies on the same arguments which were not found persuasive in the first rejection under 35 U.S.C. 103(a) set forth above.

As applied to this rejection these arguments also are not found persuasive for the same reasons as explained above and the Examiner herein incorporates the above reasoning into this rejection.

Accordingly, after considering the prior art as a whole, after carefully and fully considering Applicant's response and for the reasons of record set forth in the previous office action, the invention as a whole was obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and this rejection is maintained.

13. The rejection of claims 21, 34, 41 and 42 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,107,102 (Ferrari et al, published 2000) (of record), in view of Schlimok et al (Eur. J. Can., 31A(11):1799-1803, 1995) (of record) and Crisan et al (Molecular Diagnosis, 5(1):33-38, 2000) (of record) as applied to claims 1, 9, 13, 17, 20, 25-27, 29, 32 and 35-40 above, and further in view of US Patent No. 5,792,456 (Yelton et al, published 1998) (of record), is maintained.

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As applied to this rejection these arguments also are not found persuasive for the same reasons as explained above and the Examiner herein incorporates the above reasoning into this rejection.

Accordingly, after considering the prior art as a whole, after carefully and fully considering Applicant's response and for the reasons of record set forth in the previous office action, the invention as a whole was obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references and this rejection is maintained.

Conclusion

14. No claims are allowed.

15. Applicant's amendment necessitated the new ground(s) of objection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this supplemental final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Patent 5,624,659 (of record) teaches locally administering an antibody directed against the tumor-associated antigen, tenascin, into surgical resection cavities of glioblastoma patients during surgery. Weitz et al (Clin. Can. Res., 4:343-348, 1998, of record) teach that colorectal cancer cells are present in systemic circulation at an increased rate during surgery and suggest administering high levels of antibodies against antigens on the tumor cells during surgery to inhibit dissemination of such cancer cells. Co et al (Can Res., 56:118-1125, 1996, of record) teach a Lewis Y antibody that mediates ADCC and CDC when bound to human cancer cells.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935.

The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

/bd/
Examiner, Art Unit 1643
December 4, 2009